knees than meniscectomy only controls through 5 years. The additional tissue regeneration supported by the CMI may decrease progression of degenerative changes and reduce the necessity and frequency for additional surgeries. This study further confirms the importance of preserving as much meniscus tissue as possible at the time of meniscus surgery, and clearly it supports the potential positive benefits of regrowing or regenerating lost meniscus tissue. Our hypothesis was affirmed.

462 SIX-YEAR RESULTS WITH COLLAGEN MENISCUS IMPLANTS (CMI) WITH EMPHASIS ON LOCATION AND AMOUNT OF MENISCUS REMAINING

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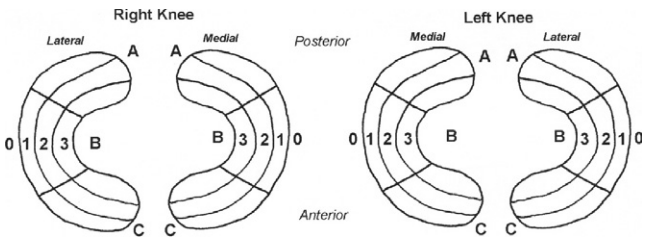
Purpose: Prospectively, we determined amount of meniscus loss and anatomic location of Collagen Meniscus Implant (CMI) placement after partial medial meniscectomy, then at 1-year relook we determined total meniscus tissue present based on surface area coverage. We correlated percent of meniscus and anatomic location of the original lesion with function and activity levels six years after CMI placement. We hypothesized that meniscus amount and anatomic location would influence clinical function and activity levels.
Methods: In a prospective randomized controlled multicenter clinical trial (Level of Evidence I), 114 chronic patients (1 to 3 prior partial meniscectomies on the involved meniscus) 18 to 60 years old underwent partial medial meniscectomy, and then randomly one group received a CMI to fill the meniscus defect. There were 68 meniscectomy only controls and 46 CMI patients. At index surgery, amount and anatomic location of meniscus removed and CMI placement were documented on a standard grid (Figure). Locations were categorized as posterior (A), middle (B), or anterior (C) third. A 1-year relook was done on CMI patients, and meniscus surface area coverage was measured. Patients were followed clinically for a minimum of two years and subjectively annually thereafter. Average follow-up was 69 months (range, 24 to 92). All patients completed validated questionnaires including Lysholm and Tegner scores to assess function and activity.
Results: For CMI patients, 29 had lesions which included the posterior and middle thirds (AB), and 17 had lesions involving all three zones (ABC). Lysholm scores were significantly higher in patients with AB lesions (81) compared to ABC lesions (71), $p = 0.046$. AB lesion patients also had significantly higher Tegner index (0.70) than ABC lesion patients (0.22), thus the AB patients regained more of their lost activity, $p = 0.049$. Comparing all patients with $\geqslant$60% meniscus surface area coverage, CMI patients had significantly higher Tegner index compared to controls (0.59 vs. 0.30), $p = 0.036$. No differences between treatment groups were seen in patients with <60% meniscus surface area coverage. When comparing 24 month values to those at final follow-up, controls had no change for Lysholm ($p = 0.13$) or Tegner ($p = 0.39$) scores, but CMI patients improved significantly over time for both Lysholm ($p = 0.02$) and Tegner ($p = 0.04$) scores.
Conclusions: The zone of meniscus involvement influenced clinical outcomes at 6 years in CMI patients with those whose lesions extended into all three zones doing worse than those with lesions in posterior and middle zones only. Patients with successful CMI procedures yielding $\geqslant$60% meniscus surface area coverage were significantly better than meniscectomy only controls for both clinical function and activity levels. Noteworthy, CMI patients continue to improve over time for clinical function and activity levels, but control patients do not.



463 TEMPORAL CHANGES IN PROTEOGLYCAN GENE EXPRESSION AND HISTOPATHOLOGY INDUCED IN SHEEP SHOULDER TENDONS BY ALTERED STRESS IN VIVO

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Purpose: Degeneration and tearing of rotator cuff tendon causes significant morbidity in our ageing population. Treatment options for cuff disorders are limited by a lack of information concerning the fundamental mechanisms that cause tendinopathy. Pre- and post-rupture changes are difficult to study in humans. An animal model of shoulder tendon injury has been recently established in our laboratories, whereby the pathological effects of both overstress (OS) and stress deprivation (SD) on tendons can be evaluated and potential molecular mechanism studied simultaneously.
Methods: Twenty-four 2 year-old Merino wethers had the infraspinatus tendon of one forelimb partially transected; 24 sheep had tendons exposed but not cut (sham) and 24 sheep were non-operated controls (NOC). After sacrifice of 6 animals in each group at 2, 13, 26 and 52 weeks, 2 regions of tensile tendon (defined by finite element analysis to be SD or OS following the transection) were removed from each shoulder. Tendon was formalin-fixed and processed for histology or snap frozen for subsequent total RNA extraction and real time RT-PCR using validated ovine-specific primers. Genes examined were aggrecan, versican, decorin, lumican, fibromodulin, biglycan, MMP-13 and ADAMTS-1, -4 and -5.
Results: Two weeks after transection, significant pathological changes were apparent in both SD and OS tensile tendon when compared with either NOC or sham-operated tendons (all $p < 0.05$). By 26 and 52 weeks, histopathology scores, including collagen alignment, had returned to sham levels in OS but not SD tensile tendon. Regardless of transection-induced OS or SD, proteoglycan staining in both regions significantly increased and was still elevated at 52 weeks ($p < 0.02$), by which time defined areas of chondroid metaplasia had become evident.
There was no difference in gene expression between sham and NOC. In SD tendon, expression ratios (fold change transected from sham) of versican, biglycan and lumican were significantly increased (all $p < 0.05$) and decorin and fibromodulin decreased ($p < 0.005$) at multiple time points. In OS tendons, upregulated expression of aggrecan and biglycan only became evident at 13 weeks post-transection (both $p < 0.02$), and decorin, fibromodulin and lumican were not regulated. MMP-13 (a major fibrillar collagenase) was significantly upregulated in SD ($p < 0.005$) but not OS tendon. Expression of all three ADAMTS, which would normally be implicated in aggrecan and versican proteolysis, was not significantly changed in either SD or OS tendon at any timepoint in this study.
Conclusions: Proteoglycan accumulation and chondroid metaplasia are major pathological findings in both SD and OS tensile tendon but the underlying molecular mechanisms appear to be temporally different. Excess proteoglycan may alter tendon biomechanics, increase susceptibility to tearing and inhibit repair processes. Pathological accumulation of proteoglycan, especially aggrecan and versican, in tensile tendon may be associated with lack of ADAMTS activity. This has implications for the treatment of tendinopathy, where molecular therapies that decrease aggrecan and increase ADAMTS may be beneficial. Furthermore, these results suggest that therapies aimed at decreasing ADAMTS activity in the joint to treat osteoarthritis may induce unwanted side effects in joint (and possibly other) tendons in the longterm.

464 EFFECT OF PRO-INFLAMMATORY AND IMMUNOREGULATORY CYTOKINES ON HUMAN TENOCYTES

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Purpose: Tendon injury leads to a local inflammatory response, characterized by the induction of pro-inflammatory cytokines such as interleukin (IL)-1beta and tumor necrosis factor (TNF)-alpha. Tendon healing is a time consuming process and strongly influenced by this post-traumatic inflammation. More and more evidence arose that the immunoregulatory Th2 cytokines Il-6 and Il-10 might also contribute to the complex remodelling processes observed during wound healing in connective tissues.
Since the role and interplay of pro-inflammatory and immunoregulatory cytokines in tendon remains still unclear, the aim of the present study was to analyze the effects of TNF-alpha, Il-6 and Il-10 on key parameters of